

**Supplementary Table 2. Summary of group-level statistical tests for (A)  $^{11}\text{C}$ -PiB, (B)  $^{11}\text{C}$ -DED, (C)  $^{18}\text{F}$ -FDG.**

The Kruskal-Wallis test was performed to compare the pMC, CTR, PiB+ MCI, and Alzheimer's disease groups ( $N = 5, 15, 13, 8$ , respectively). The pMC group comprised subjects aged less than the average age of onset. Arctic mutation carriers in the pMC group were excluded from the  $^{11}\text{C}$ -PiB retention statistical comparisons. Results of the Kruskal-Wallis test are reported as test statistic H (df), where df = 3 is the number of degrees of freedom, followed by the significance value (p); results are shown only for those ROIs for which the Kruskal-Wallis test was significant. Results of Mann-Whitney U tests are reported as the significance value (p) and effect size (r) for each pair of diagnostic groups. The CTR groups were composed of non-carrier members of ADAD families ( $n=16$ ) for  $^{11}\text{C}$ -PiB and  $^{18}\text{F}$ -FDG PET, and healthy subjects ( $n=14$ ) for  $^{11}\text{C}$ -DED PET. The threshold for statistical significance was set at  $p = 0.05$ . All statistical results that survived multiple comparisons correction are indicated in bold.

CTR = control;  $^{11}\text{C}$ -DED = deuterium-L-deprenyl;  $^{18}\text{F}$ -FDG = fluorodeoxyglucose; MCI = mild cognitive impairment; ns = not significant;  $^{11}\text{C}$ -PiB = Pittsburgh Compound-B; pMC = presymptomatic mutation carrier.

**A**

Regions of Interest	<sup>11</sup> C-PIB retention		<sup>11</sup> C-PIB retention				
	Kruskal-Wallis H(3) (p value)		Mann-Whitney U test statistic			(p value)	(effect size r)
	pMC, PiB+ MCI, Alzheimer's disease, CTR	pMC vs CTR	pMC vs PiB+ MCI	pMC vs Alzheimer's disease	PiB+ MCI vs CTR	PiB+ MCI vs Alzheimer's disease	Alzheimer's disease vs CTR
<u>Cortical regions</u>							
Frontal cortex	<b>32.40</b> (p<0.001)	3 (p=0.003) (r=0.67)	9 (p=0.021) (r=0.55)	1 (p=0.005) (r=0.77)	0 (p<0.001) (r=0.85)	18 (p=0.014) (r=0.54)	0 (p<0.001) (r=0.81)
Parietal cortex	<b>31.79</b> (p<0.001)	6 (p=0.006) (r=0.61)	4 (p=0.005) (r=0.66)	0 (p=0.003) (r=0.81)	0 (p<0.001) (r=0.85)	ns	0 (p<0.001) (r=0.81)
Temporal cortex	<b>31.86</b> (p<0.001)	5 (p=0.005) (r=0.63)	3 (p=0.004) (r=0.69)	0 (p=0.003) (r=0.81)	0 (p<0.001) (r=0.85)	ns	0 (p<0.001) (r=0.81)
Occipital cortex	<b>29.27</b> (p<0.001)	9 (p=0.013) (r=0.56)	9 (p=0.021) (r=0.55)	1 (p=0.005) (r=0.77)	2 (p<0.001) (r=0.83)	ns	0 (p<0.001) (r=0.81)
Anterior cingulate cortex	<b>29.89</b> (p<0.001)	11 (p=0.021) (r=0.52)	12 (p=0.043) (r=0.48)	2 (p=0.008) (r=0.73)	0 (p<0.001) (r=0.85)	26 (p=0.060) (r=0.41)	0 (p<0.001) (r=0.81)
Posterior cingulate cortex	<b>30.85</b> (p<0.001)	8 (p=0.010) (r=0.58)	6 (p=0.009) (r=0.62)	2 (p=0.008) (r=0.73)	0 (p<0.001) (r=0.85)	ns	0 (p<0.001) (r=0.81)
Insular cortex	<b>31.25</b> (p<0.001)	6 (p=0.006) (r=0.61)	7 (p=0.012) (r=0.59)	1 (p=0.005) (r=0.77)	0 (p<0.001) (r=0.85)	ns	0 (p<0.001) (r=0.81)
Parahippocampus	<b>25.74</b> (p<0.001)	ns	11 (p=0.034) (r=0.50)	5 (p=0.028) (r=0.61)	6 (p<0.001) (r=0.80)	ns	0 (p<0.001) (r=0.81)
<u>Subcortical regions</u>							
Caudate nucleus	<b>26.41</b> (p<0.001)	7 (p=0.008) (r=0.60)	ns	ns	0 (p<0.001) (r=0.85)	ns	0 (p<0.001) (r=0.81)
Putamen	<b>27.53</b> (p<0.001)	10 (p=0.016) (r=0.54)	ns	ns	0 (p<0.001) (r=0.85)	24 (p=0.043) (r=0.44)	0 (p<0.001) (r=0.81)
Thalamus	<b>24.84</b> (p<0.001)	11 (p=0.021) (r=0.52)	ns	ns	1 (p<0.001) (r=0.84)	ns	0 (p<0.001) (r=0.81)

**B**

Regions of Interest	<sup>11</sup> C-DED binding Mann-Whitney U test (p value) (effect size r)						
	pMC, PiB+ MCI, Alzheimer's disease, CTR	pMC vs CTR	pMC vs PiB+ MCI	pMC vs Alzheimer's disease	PiB+ MCI vs CTR	PiB+ MCI vs Alzheimer's disease	Alzheimer's disease vs CTR
<u>Cortical regions</u>							
Frontal cortex	8.50 (p=0.037)	<b>5</b> <b>(p=0.005)</b> <b>(r=0.64)</b>	ns	ns	54 (p=0.073) (r=0.35)	ns	29 (p=0.065) (r=0.39)
<u>Subcortical regions</u>							
Thalamus	<b>10.20</b> <b>(p=0.017)</b>	9 (p=0.016) (r=0.55)	11 (p=0.034) (r=0.50)	3 (p=0.013) (r=0.69)	ns	28 (p=0.082) (r=0.38)	ns

**C**

Regions of Interest	<sup>18</sup> F-FDG uptake Kruskal-Wallis H(3) (p values)		<sup>18</sup> F-FDG uptake Mann-Whitney U test statistic (p value) (effect size r)				
	pMC, PiB+ MCI, Alzheimer's disease, CTR	pMC vs CTR	pMC vs PiB+ MCI	pMC vs Alzheimer's disease	PiB+ MCI vs CTR	PiB+ MCI vs Alzheimer's disease	Alzheimer's disease vs CTR
<u>Cortical regions</u>							
Frontal cortex	<b>17.72</b> (p<0.001)	ns	9 (p=0.021) (r=0.55)	4 (p=0.019) (r=0.65)	<b>30</b> (p=0.001) (r=0.60)	ns	<b>12</b> (p=0.001) (r=0.65)
Parietal cortex	<b>23.38</b> (p<0.001)	ns	10 (p=0.027) (r=0.52)	<b>0</b> (p=0.003) (r=0.81)	<b>23</b> (p<0.001) (r=0.66)	26 (0.060) (r=0.41)	<b>3</b> (p<0.001) (r=0.76)
Temporal cortex	<b>26.06</b> (p<0.001)	ns	6 (p=0.009) (r=0.62)	<b>1</b> (p=0.005) (r=0.77)	<b>11</b> (p<0.001) (r=0.76)	ns	<b>2</b> (p<0.001) (r=0.78)
Occipital cortex	<b>10.24</b> (p=0.017)	ns	ns	ns	<b>39</b> (p=0.004) (r=0.53)	ns	28 (p=0.028) (r=0.45)
Anterior cingulate cortex	<b>12.22</b> (p=0.007)	ns	ns	4 (p=0.019) (r=0.65)	<b>42</b> (p=0.007) (r=0.50)	ns	<b>20</b> (p=0.007) (r=0.55)
Posterior cingulate cortex	<b>23.01</b> (p<0.001)	ns	13 (p=0.055) (r=0.45)	4 (p=0.019) (r=0.65)	<b>17</b> (p<0.001) (r=0.71)	ns	<b>3</b> (p<0.001) (r=0.76)
Insular cortex	<b>18.27</b> (p<0.001)	ns	8 (p=0.016) (r=0.57)	4 (p=0.019) (r=0.65)	<b>27</b> (p<0.001) (r=0.63)	ns	<b>12</b> (p=0.001) (r=0.65)
Parahippocampus	<b>14.36</b> (p=0.002)	ns	7 (p=0.012) (r=0.59)	5 (p=0.028) (r=0.61)	<b>36</b> (p=0.003) (r=0.55)	ns	22 (p=0.010) (r=0.53)
<u>Subcortical regions</u>							
Caudate nucleus	<b>16.24</b> (p=0.001)	ns	<b>5</b> (p=0.007) (r=0.64)	3 (p=0.013) (r=0.69)	<b>35</b> (p=0.002) (r=0.56)	ns	<b>18</b> (p=0.005) (r=0.58)
Putamen	8.22 (p=0.042)	ns	12 (p=0.043) (r=0.48)	ns	45 (p=0.010) (r=0.48)	ns	ns
Thalamus	<b>22.46</b> (p<0.001)	ns	<b>1</b> (p=0.002) (r=0.73)	<b>0</b> (p=0.003) (r=0.81)	<b>34</b> (p=0.002) (r=0.57)	ns	<b>6</b> (p<0.001) (r=0.73)
Hippocampus	<b>19.07</b> (p<0.001)	ns	<b>5</b> (p=0.007) (r=0.64)	3 (p=0.013) (r=0.69)	<b>25</b> (p<0.001) (r=0.64)	ns	<b>15</b> (p=0.003) (r=0.61)